The association between sex and body size and stroke risk and survival in patients with atrial fibrillation – an analysis of 71,589 patients from the COMBINE-AF study

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Background:

In patients with atrial fibrillation (AF), the risk of stroke is higher and mortality is lower in females than males. Whether a smaller body size in female patients is associated with outcomes is uncertain. We assessed the risk of stroke/systemic embolism (SE), major bleeding, cardiovascular (CV) death and all-cause death in females vs males in patients with AF treated with a DOAC or warfarin, and sought to determine whether the risks are modified by demographics and clinical characteristics including weight and height.

Methods:

We used pooled patient-level data from 4 large RCTs investigating DOACs vs warfarin (ARISTOTLE, ENGAGE AF-TIMI 48, RE-LY, ROCKET) from the COMBINE-AF cohort.

Stepwise Cox-regression analyses were used to adjust for factors modifying the associations with outcomes. Four models were constructed as follows:

Model 0: no adjustment;

Model 1: age+trial+randomized treatment;

Model 2A: model 1+prior stroke/TIA+heart failure+diabetes+hypertension+vascular disease;

Model 2B: model 1+creatinine+weight+height+weight*height

Results:

Data were available for 71,589 patients (26,659 females). Median age was 73 and 71 years, median height 160 and 174 cm, median weight 73.0 and 85.3 kg in females and males, respectively. During 2.3 years median follow-up, there were 2,494 stroke /SE, 1,960 ischemic stroke/SE, 648 intracranial bleeding, 1,584 gastrointestinal (GI) bleeding, 3,660 CV death, and 5,818 all-cause death. In Cox models, female sex was not independently associated with stroke after adjustment for height and weight (Table). Female sex was independently associated with less bleeding and, with greater magnitude after adjustment for height and weight, lower mortality (Table).

Conclusions:

In patients with AF treated with an OAC, females have higher rate of stroke than males but there is no independent association between female sex and risk of stroke/SE after adjustment for weight and height. Females have less bleeding and lower mortality than males, which remains significant even after adjustment for clinical factors.

Opportunistic Versus Systematic Atrial Fibrillation Screening in Primary Care: Results From the STROKESTOP III Trial

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Background:

Screening for atrial fibrillation (AF) can identify undiagnosed AF and reduce stroke risk. Participation has been low in studies employing population screening. Opportunistic screening during primary care visits could improve participation.

Methods:

STROKESTOP III was a cluster-randomized trial including 16 primary care centers allocated to either systematic screening (n=8) or opportunistic screening (n=8). Individuals born in 1948–1949 were eligible. In the systematic arm, individuals were invited by mail, whereas invitations in the opportunistic arm were issued during routine primary care visits. Exclusion criteria included known AF, ongoing anticoagulant treatment, and dementia. Eligible participants performed intermittent single-lead 30-second ECG recordings three times daily for two weeks using a handheld device.

Results:

The study was initiated in May 2024 and concluded in October 2025. In total, 2969 patients were registered across the 16 primary care centers. In the opportunistic arm, 1 476 individuals were allocated, of whom 818 attended a primary care visit and were assessed for eligibility. Among these, 148 (18.1%) fulfilled exclusion criteria, leaving 670 eligible individuals, of whom 374 participated (55.8%).

In the systematic screening arm, 1 436 individuals were allocated. A total of 171 (11.9%) met exclusion criteria, leaving 1 265 eligible individuals, of whom 607 participated (48.0%). Participation among invited individuals was significantly higher in the opportunistic screening arm compared with the systematic arm ($p<0.005$). Participants in the opportunistic arm had a higher mean CHA_2DS_2-VASc score (4.0, $p<0.005$) and a higher prevalence of AF risk factors, including hypertension and diabetes (Table 1). AF detection was low in both arms, with 3 cases (0.8%) detected in the opportunistic arm and 8 cases (1.3%) in the systematic arm ($p=0.54$).

Conclusion:

Opportunistic AF screening achieved higher participation rate and included individuals with a higher cardiovascular risk profile compared with systematic screening, while AF detection remained low in both strategies.

Magnetic resonance stress-perfusion comparison in patients with Fontan circulation of left- or right systemic ventricular morphology

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Background: In patients with Fontan circulation, a single ventricle is responsible for both systemic and pulmonary circulations which limits the heart's capacity to augment CO during periods of increased metabolic demand, mainly because of increased central venous pressure and decreased diastolic filling. The objectives of this study were to; 1) test feasibility and safety of adenosine stress-perfusion; 2) compare stress-perfusion, perfusion reserve, and global longitudinal strain (GLS) in left- (LV) versus right (RV) ventricular morphology and 3) explore the relationship between stress-perfusion and maximal oxygen consumption (VO2 max).

Method: Patients with Fontan circulation (n=28, median age=25 (95% CI, 21.9 to 28.1), 46% female) were prospectively enrolled between April 2024 and June 2025. The cohort was stratified into two groups based on LV or RV ventricle morphology. All imaging were performed using a 1.5T magnetic resonance scanner using first-pass perfusion imaging during adenosine infusion at 110 µg/kg/min, with titration up to 170 µg/kg/min if necessary. Cardiopulmonary exercise testing was conducted to assess VO2 max.

Results: 16 patients, 25 years old (95% CI, 20.3 to 29.7), n=8 (50%) female) had LV morphology and 12 patients, 26 years old (95% CI, 21.0 to 30.0), n=5 (42%) female) had RV morphology. All recruited patients completed the MR study protocol. Analysis showed better GLS (p=0.003) and a trend to higher systemic EF (p=0.07) in patients with LV morphology. There was no significant difference in perfusion during stress (p=0.19), rest (p=0.24) and perfusion reserve (p=0.87) between the groups. No significant correlations were observed between stress-perfusion or perfusion reserve regarding VO2 max.

Conclusions: Adenosine quantitative stress-perfusion was feasible and safe with no serious adverse events. Ventricular morphology did not affect perfusion, but GLS was significantly better in patients with LV morphology. VO2 max did not differ between ventricular morphology and perfusion was not related to VO2 max.

Descending Aortic Regurgitation Fraction as a Quantitative Hallmark of Severe Aortic Regurgitation

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Introduction

Accurate quantification of aortic regurgitation (AR) severity is essential for risk stratification and timing of intervention. While cardiovascular magnetic resonance (CMR)–derived regurgitation fraction (RF) measured proximally is established, the clinical relevance of quantitatively assessed descending aortic RF remains uncertain.

Methods

This retrospective observational study included 106 patients with chronic AR who underwent transthoracic echocardiography and CMR. RF was quantified by phase-contrast CMR at the sinotubular junction, proximal ascending aorta, and descending thoracic aorta. Associations between RF and symptoms (NYHA class), NT-proBNP levels, and CMR-derived ventricular remodeling and function were analyzed. Receiver-operating characteristic (ROC) analyses evaluated RF for identifying clinically significant AR using surgical decision-making and a composite clinical severity endpoint as references. A descending aortic RF threshold was derived and used for patient stratification. Analyses of symptoms, biomarkers, and remodeling excluded patients with atrial fibrillation, cardiomyopathy, prior myocardial infarction, or more than moderate mitral regurgitation.

Results

RF measured at the sinotubular junction and descending thoracic aorta showed excellent discrimination for surgical decision-making (AUC 0.97 and 0.96). For the composite clinical endpoint, descending aortic RF demonstrated slightly higher discrimination than proximal RF (AUC 0.75 vs 0.74). A descending aortic RF threshold of 23% emerged as optimal and correlated strongly with a sinotubular junction RF ≥32% (r = 0.82). Patients with descending RF ≥23% had more advanced ventricular remodeling, higher NT-proBNP levels, greater symptom burden, and more frequent holodiastolic flow reversal, with nearly 90% undergoing surgery. Only 11% of patients with descending RF <23% underwent surgery, mainly for alternative guideline-supported indications.

Conclusion

CMR-derived descending thoracic aortic regurgitation fraction is closely associated with symptoms, biomarker elevation, and left ventricular remodeling in chronic AR. A threshold of ≥23% provides complementary information to established proximal measurements and may help identify hemodynamically significant disease when integrated with comprehensive clinical and imaging assessment in clinical practice.

Percutaneous closure of patent foramen ovale after cryptogenic stroke – a comparison between patients younger and older than 60 years

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Background

Cryptogenic ischemic stroke is strongly associated with patent foramen ovale (PFO). Current guidelines recommend percutaneous PFO closure in patients <60 years-of-age. This study aimed to compare the incidences of recurrent stroke or transient ischemic attack (TIA), and atrial fibrillation after percutaneous PFO closure in patients aged >60 years with patients <60 years-of-age.

Methods

This retrospective study included all adult Swedish patients with cryptogenic stroke treated with percutaneous closure of PFO 2001-2023. Patient characteristics and procedural details were obtained from the Swedish registry of adult congenital heart disease. Preprocedural atrial fibrillation and post-procedural incidence of recurrent cerebral infarction, TIA, and atrial fibrillation were obtained from the Swedish National Board of Health and Welfare's registry of patient diagnoses. To compare differences across age groups, logistic-, quantile-, and linear regression models were used. P-values <0.050 were considered significant.

Results

In total, 1,101 patients were included with follow-up time 7.1 ± 5.8 years, of which 12% (n=134) were >60 years-of-age. Low prevalence of preprocedural comorbidity was seen in both age groups and there was no difference in incidence of atrial fibrillation within 3 months after PFO closure (>60 years-of-age n= 4, 3.0%, <60 years-of-age n= 23, 2.4%, p=0.229), or recurrent cerebral infarction/TIA (>60 years-of-age n= 3, 2.7%, <60 years-of-age n= 17, 1.5%, p=0.697) between the age groups.

Conclusions

This nation-wide study showed low incidence of recurrent stroke, peripheral embolization, and 3-month post-procedural atrial fibrillation after percutaneous PFO closure in patients aged 60 years and older, with no increased incidence of recurrent stroke or TIA compared with patients <60 years-of-age. These findings suggest percutaneous PFO closure can be considered a safe and efficient therapy in the reduction of recurrent stroke in patients older than 60 years with low preprocedural comorbidity.

Standardized, telemonitored titration of guideline-directed medical therapy in heart failure is associated with faster optimization and improved persistence

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Background

Delayed initiation and incomplete up-titration of guideline-directed medical therapy (GDMT) remain common in heart failure with reduced ejection fraction (HFrEF) and are associated with poor outcomes. We evaluated whether a fully standardized, home-based titration strategy supported by telemonitoring improves dose attainment and treatment persistence compared with contemporary standard care.

Methods

This study compares a previously published prospective cohort of patients enrolled in a standardized, protocol-driven home-based titration program (TELEFASTER-HF) with a retrospectively identified control cohort treated during the same period. Patients had newly diagnosed or decompensated HFrEF and identical eligibility criteria. Controls were identified from routine care at Sahlgrenska University Hospital. Baseline differences were addressed using inverse probability of treatment weighting (IPTW) based on 23 predefined covariates. The primary endpoint was GDMT dose distribution at 8 weeks. Secondary outcomes included GDMT target attainment, time to OMT, and change in eGFR.

Results

A total of 126 patients were included (60 intervention, 66 controls). At 8 weeks, the distribution of dose categories differed significantly between groups across all guideline-directed medical therapy classes, with a substantially higher proportion of patients in the intervention group reaching higher dose categories ($p<0.001$), Fig 1. Achievement of target doses in all four drug classes occurred in 65% of intervention patients compared with 10% of controls (odds ratio 14.3, 95% confidence interval 4.7–43.3; $p<0.001$). Time to optimal medical therapy was markedly shorter in the intervention group (hazard ratio 13.4, 95% confidence interval 6.5–27.4; $p<0.001$), Fig 2. There was no difference in eGFR between groups.

Conclusions

A standardized, home-based titration strategy achieved faster and more advanced GDMT dose escalation than standard care in HFrEF. These findings support protocol-driven approaches to address persistent implementation gaps in routine HF management.

Impact of Preoperative Pulmonary Artery Systolic Pressure on Outcomes After Mitral Valve Repair for Degenerative Mitral Regurgitation

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Background:Pulmonary artery systolic pressure (PASP)>50mmHg, indicating significant pulmonary hypertension, is one of the guideline criteria for mitral valve (MV) surgery in degenerative mitral regurgitation (DMR). Aim:To assess the prevalence, clinical profile, and outcomes of contemporary patients with elevated PASP undergoing MV repair for DMR.

Methods:Consecutive patients with moderate-to-severe DMR due to MV prolapse (MVP) who underwent MV repair at Karolinska University Hospital between 2010-2024 were included. Those with mitral stenosis, rheumatic MV disease, endocarditis, prior MV surgery, secondary MR or missing baseline PASP were excluded. PASP was estimated from echocardiography and categorized as substantially increased (>50mmHg) or not substantially increased (≤50mmHg). Data were extracted from electronic medical records and echocardiograms. Outcomes were assessed as time to first event in Kaplan–Meier analysis.

Results:Among 608 patients, 124 (20.4%) had PASP>50mmHg, median [IQR]: 60[55-70]mmHg, and 484 (79.6%) had PASP≤50mmHg, median: 35[28-41]mmHg. Patients with PASP>50mmHg were older, more often in NYHAclass III-IV and had higher left atrial volume index, more frequently LVEF<50% and moderate-to-severe tricuspid regurgitation (TR). There was no difference in baseline MR severity between the groups. Patients with PASP>50mmHg had less often anterior leaflet prolapse or bileaflet prolapse, and underwent more often concomitant CABG and tricuspid valve interventions. PASP>50mmHg was associated with higher rates of residual TR, prolonged mechanical ventilation (>2days) and ECMO support as well. During a median follow-up of 5[1-9]years, patients with PASP>50mmHg had higher crude risks of death, heart failure hospitalization, permanent pacemaker implantation and myocardial infarction (figure). No significant associations were observed with endocarditis, stroke, and mitral valve reoperation for repair failure.

Conclusions:In patients undergoing MV repair for DMR due to MVP, 20.4% had substantially elevated PASP preoperatively. Elevated PASP was associated with worse preoperative status, more complex surgical procedures, higher risk of worse in-hospital and long-term outcomes, supporting referral for surgery before substantial increases in PASP occur.

Survival after aortic valve surgery for prosthetic valve endocarditis: a SWEDEHEART study

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Background: An increasing number of people live with aortic prosthetic valves. Over time, up to 10% of them may develop prosthetic valve endocarditis (PVE) – a serious and life-threatening complication. Cardiac surgery is needed in the majority of patients with PVE, yet data on outcomes after surgery are scarce.

Aim: To examine outcomes after aortic valve surgery for PVE.

Methods: We conducted a population-based, observational cohort study using data from SWEDEHEART and other national health registries. All patients receiving aortic valve surgery for endocarditis in Sweden 1997–2022 were included. The Kaplan Meier method and regression standardization were used to compare long-term survival among patients who lived past 30 days after surgery, comparing PVE and native valve endocarditis (NVE).

Results: Among 2585 patients, 685 (26%) had PVE and 1900 (74%) had NVE. PVE patients were older (68 vs. 61 years) and had more comorbidities than NVE patients. Mean follow-up was 7.1 years (maximum 26 years). Thirty-day mortality was higher among PVE (12%) than NVE (6.1%) patients; adjusted odds ratio 1.76 (95% CI: 1.20-2.59). Long-term survival was similar for PVE and NVE among patients who lived past 30 days after surgery; absolute survival difference at 10 years was -4.6% (95% CI: -10.4 to 1.5).

Conclusions: While PVE patients had higher short-term mortality, patients who survived 30 days after surgery had a similar 10-year prognosis to NVE patients. These results are encouraging and suggest that good long-term outcomes are achievable after surgery for PVE.

BLOOD PRESSURE FIVE YEARS AFTER RADIOFREQUENCY RENAL DENERVATION IN UNCONTROLLED HYPERTENSION: THE SWEDISH REGISTRY FOR RENAL DENERVATION

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Background

Renal denervation (RDN) is a complementary treatment option for uncontrolled hypertension. Studies on sustained long-term blood pressure (BP) reduction are few. We here report on sustained 5-year BP reductions from the Swedish Registry for Renal Denervation.

Methods

All RDN procedures in Sweden are included in a national registry. We evaluated all 83 patients undergoing radiofrequency in our institution 2011–25 for uncontrolled (resistant or drug intolerance) hypertension. Follow-up were scheduled at 6, 12, 24, 36, 48, and 60 months. Estimated means ± SE or 95% CL are shown. Linear mixed□effects models were used, adjusted for age and number of antihypertensive drugs.

Results

Mean age was 58±13, 41% were female, 39% previous and 11% current smokers, 21% had diabetes, 19% chronic kidney disease, 5 % heart failure, and 22% coronary artery disease or a previous TIA/stroke. Baseline office BP and average 24-h ABPM were 178±3 / 96±2 and 154±3 / 88±2 mm Hg, eGFR 74 ml/min/m2, and number of antihypertensive drugs 3.7±0.3. Office SBP was reduced ranging from –11 (–3 to –18; p<0.001) at 6 months to –32 (–21 to –44; p<0.001) at 60 months. Office DBP was reduced ranging from -2 (+2 to –4; p=1.0) to -12 (–4.6 to –19.2; p<0.001). Systolic ABPM showed reduced BP ranging from -2 (+3 to -12; p=1.0) at 6 months to -14 (-6 to -21; p<0.001) at 36 months. Diastolic ABPM showed reduced BP ranging from -1 (+2 to -3; p=1.0) at 6 months to -8 (-3 to¬ -13; p<0.01) at 36 months. This study indicates overall sustained 5-year reductions of office and average 24-h ABPM values. Number of antihypertensive drugs remained similar, 3.8±0.3 at 60 months. There was a small decline in eGFR, -9±2 ml/min/m2 at 60 months.

Conclusions

Radiofrequency RDN offers sustained 5-year BP reductions in patients with uncontrolled hypertension.

Prevalence and diagnostic trends of spontaneous coronary artery dissection (SCAD) in young women- a multicentre angiographic review.

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Background

Previous studies suggest that SCAD may account for up to 35% of all acute coronary syndrome cases in young women (<50 y). In Sweden, the prevalence of SCAD remains unclear as does the evolution of diagnostic trends over time.

Method

We retrospectively reviewed all invasive coronary angiograms (ICA) 2015 - 2023 in women < 50 years with suspect myocardial infarction (MI) at three Swedish hospitals. Data were retrieved from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and supplemented with medical records. Two independent reviewers re-evaluated all ICAs. SCAD prevalence based on angiographic review was compared to SCAAR and medical records. Sensitivity, specificity and inter-observer agreement (κ) and temporal trends in diagnostic agreement were analysed.

Results

In all 265 women underwent ICA for suspected MI whereof 56 SCAD cases were identified on angiographic review (21.1 %).

In SCAAR, the SCAD variable was completed in 165 cases (62%), with 32 SCAD cases reported as SCAD (19.4 %, 80.2% sensitivity, 98.2% specificity). Agreement between registry data and angiographic review was moderate (κ = 0.62) with a clear improvement over time (yearly κ values range 0.28-0.89, β coefficient=0.706, p= 0.051).

In medical files, SCAD was documented in 38 patients (14.3 %, 66.6% sensitivity, 98.9% specificity) with a moderate inter-observer agreement (κ=0.61) and an improvement over time (κ range 0.129-1.00, β coefficient = 0.784, p = 0.012).

Conclusion

SCAD was underdiagnosed in the SCAAR registry and clinical documentation during the early study period, but diagnostic recognition improved over time. In contemporary Swedish women < 50 years of age with myocardial infarction, SCAD accounted for approximately one in five cases.

Prevalence and prognostic importance of chronic kidney disease in patients with coronary heart disease: Results from the INTERASPIRE survey from 14 countries across six WHO regions

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Background: Chronic Kidney Disease (CKD) is a major risk factor for the progression of coronary artery disease (CAD). The study aimed to determine the prevalence of CKD among CAD patients across 14 countries in all WHO regions and to assess the prognostic value of estimated glomerular filtration rate (eGFR) and urinary albumin/creatinine ratio (UACR)

Methods: A total of 4,548 patients with CAD were included (79.6% male; age range 18-80 years). They were assessed with eGFR and UACR 6-24 months after the diagnosis of CAD. Complete information on kidney function and cardio-renal protective therapy was available in 3,865 patients and follow up data after a median of one year in 3,577 (92.5%).

Results: CKD according to the Kidney Disease Improving Global Outcomes (KDIGO) classification was present in 32% of whom 19.7% were classified as low-moderate, 6.9% as high, and 5.6% as very high risk. Without UACR 51.3% of them would have been undetected. The primary event, first of cardiovascular death, myocardial infarction, stroke, and hospitalisation for heart failure, was observed in 7.9% with the highest incidence in the KDIGO high risk group (men 13.0%, women 11.8%). This relationship was independent of other risk factors and evident soon after the index examination. Only a minority of the patients received adequate cardio-reno-protective therapy.

Conclusions: Early screening for CKD in patients with CAD is important and must include both eGFR and UACR to provide adequate information. Without UACR half of those with CKD would remain undetected. Treatment with lifesaving, cardio-renal protective therapy was low indicating a great improvement potential.

Long-term antiplatelet treatment in type 2 myocardial infarction – a target trial emulation study

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Background

Type 2 myocardial infarction (MI) is associated with high mortality, yet no evidence-based treatments have been established. Despite limited evidence, antiplatelet therapy is often prescribed after type 2 MI. Target trial emulation has emerged as a recognized approach for estimating treatment effects using observational data when randomized clinical trials are difficult to conduct.

Purpose

To assess whether initiation of antiplatelet therapy improves survival and reduces cardiovascular events in patients with type 2 MI without other clear indications.

Methods

Two hypothetical target trials were designed and emulated using Swedish observational registry data: one evaluating the intention to treat effect of initiating single antiplatelet therapy (SAPT) vs. no SAPT and one evaluating initiation of dual antiplatelet therapy (DAPT) vs. no DAPT. The primary outcome was a composite of time to all-cause death, readmission for MI, stroke or heart failure. Inverse probability weighting was used to adjust for confounding factors.

Results

A total of 12,889 patients reported as type 2 MI in the SWEDEHEART registry between September 3, 2010, and June 30, 2021, and discharged alive were included. After exclusion of patients with other indications or contraindications according to the eligibility criteria of the corresponding target trial, 2,178 and 5,062 patients were eligible for the SAPT and DAPT trial emulations respectively.

• SAPT was initiated in 1,144 and not initiated in 1,034 patients with no significant difference in the composite endpoint (adjusted HR: 1.04; 95% CI: 0.89 – 1.22; P = 0.63).

• DAPT was initiated in 1,724 and not initiated in 3,338 patients with no significant difference in the composite endpoint (adjusted HR: 1.02; 95% CI: 0.93 – 1.13; P = 0.63).

Conclusion

Routine initiation of antiplatelet therapy in patients with type 2 MI does not seem to confer prognostic benefit. Treatment decisions should instead be guided by established clinical indications.

Automated medical history-based HEART score for one-year major adverse cardiovascular events after acute chest pain evaluation

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Background

Automated medical history (AMH) may enable scalable, patient-driven risk stratification of chest pain patients to guide follow-up after emergency department (ED) evaluation. While the HEART score is validated for 30-day major adverse cardiac events (MACE), its performance beyond 30-days is less established. We evaluated whether a patient-generated AMH-based HEART score predicts 1-year MACE.

Methods

In this prospective cohort study, patient-reported medical histories were collected at Danderyd Hospital ED (2017-2019) using an AMH software (Clinical Expert Operating System, CLEOS, Figure 1). Clinically stable adults, presenting with non-diagnostic ECG and/or biomarkers were included; patients with MACE at the index visit (day 0) were excluded. Treating physicians were blinded to patient responses and provided standard care. The primary outcome was 1-year MACE, defined as all-cause death, acute myocardial infarction or revascularization occurring 1–365 days after the index visit. History and risk factor components of HEART were derived from AMH (Figure 2); age, ECG, troponin values, and outcomes were obtained from the electronic health record. Prognostic performance was assessed for rule-out (HEART score ≤3) and increased-risk classification (HEART >3).

Results

Among 941 included patients (Table 1), HEART score was calculable in 694 (73.9%). One-year MACE occurred in 15/694 (2.2%; Figure 3). Low risk classification (HEART ≤3) comprised 413/694 (59.5%); 1 patient (0.2%) experienced MACE, corresponding to a negative predictive value of 99.8% (95% CI 98.7–100). Among patients with HEART score >3, 14/281 (5.0%) experienced MACE, with a sensitivity of 93.3% (95% CI 68.1–99.8). Area under the receiver operating characteristic curve was 0.80 (95% CI 0.74–0.85).

Conclusions

A patient-generated AMH-based HEART score demonstrated excellent rule-out performance for 1-year MACE and acceptable discrimination for identifying patients at increased risk after ED discharge. These findings support AMH as a scalable complement to acute chest pain management, warranting further external validation.

Proteomic Signatures of Cardiovascular Resilience in Long-standing Type 1 Diabetes

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Background: Cardiovascular disease remains the leading cause of mortality in Type 1 diabetes. However, a unique subset of individuals, termed "Escapers", remains free from macrovascular and renal complications despite decades of glycemic exposure. We hypothesized that this survival is driven by active protective mechanisms, or cardiovascular resilience, rather than merely the absence of traditional risk factors.

Methods: In this cross-sectional exploratory study, we utilized a targeted proteomic approach (Olink Cardiovascular III) to analyse plasma from the ESCAPER cohort, recruited at Skåne University Hospital, Sweden. This group comprises 113 individuals with Type 1 diabetes duration >30 years who remain free from major complications. To isolate signals of resilience, they were contrasted against an extreme phenotype of 58 "Rapid Progressors" (short, multiple cardiovascular/renal complications) derived from the Swedish PROLONG study. Differences in protein levels were assessed using linear regression models adjusted for age, sex, estimated glomerular filtration rate, and glycated hemoglobin levels.

Results: In the fully adjusted model, 20 proteins were significantly differentially expressed. Rapid Progressors exhibited markedly elevated levels of the apoptotic marker Caspase-3 ($p<0.0001$) and adhesion molecules including Junctional Adhesion Molecule A and P-Selectin ($p<0.0001$), indicating upregulated apoptotic signaling and vascular inflammation. Additionally, the DNA-repair enzyme Bleomycin Hydrolase was elevated in this group. In contrast, only two proteins displayed the opposite pattern with significantly higher levels in Escapers: von Willebrand Factor (-1.36 NPX, $p<0.0001$) and Paraoxonase 3 ($p=0.003$).

Conclusions: Cardiovascular resilience in Type 1 diabetes is characterized by suppressed apoptotic signaling and dampened endothelial inflammation. We propose that the paradoxical preservation of von Willebrand Factor and Paraoxonase 3 levels in Escapers reflects maintained endothelial capacity and antioxidative defense, whereas the lower levels in progressors may result from consumption and depletion in the damaged vasculature.

Lipid management in high cardiovascular risk patients without prior myocardial infarction or stroke

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Background: Lipid-lowering therapy (LLT) improves cardiovascular outcomes in high-risk individuals, but real-world data on LLT use and low-density lipoprotein cholesterol (LDL-C) target attainment in routine clinical practice remain limited.

Methods: This retrospective cohort study used Swedish health records (2017–2024) to identify individuals aged ≥50 years with LDL-C ≥2.3 mmol/L considered at high cardiovascular risk based on having established atherosclerotic cardiovascular disease (ASCVD; coronary, peripheral, or cerebrovascular) and/or high-risk diabetes mellitus (high-risk DM; defined as presence of microvascular complications or chronic insulin use). Patients with prior myocardial infarction, stroke, or end-stage renal disease were excluded. Two patient groups were assessed: i) ASCVD with or without high-risk DM and, ii) high-risk DM without ASCVD. LDL-C levels and latest LLT use within two years post index were summarized.

Results: Of 106,698 patients, 72% (n=77,199) had at least two years of follow-up, 62% had ASCVD and 38% had high-risk DM without ASCVD at baseline (Table 1). Baseline LLT use was 39% in the ASCVD cohort and 48% in the high-risk DM cohort (Figure 1). Within two years, 24% of patients in the ASCVD cohort intensified LLT and 57% of LLT-naïve patients at baseline initiated therapy (Figure 1). Follow-up LDL-C measurement within two years was available in 67% of patients, of whom 27% achieved LDL-C target <1.8 mmol/L. In the high-risk DM cohort, 14% intensified LLT and 47% initiated therapy during follow-up (Figure 1). LDL-C was measured in 85%, with 23% achieving target. LLT intensification mainly involved increase in statin intensity. Ezetimibe use was low (<5%) and PCSK9i use was negligible (Figure 1).

Conclusion: Despite strong evidence supporting LLT in high-risk patients, real-world use, treatment intensification, and achievement of LDL-C targets were low among high-risk patients, highlighting opportunities to improve cardiovascular prevention.

Reclassification of Physiological Risk Using the Updated European Respiratory Society and European Society of Thoracic Surgeons Cardiopulmonary Exercise Testing Guideline

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Background

Cardiopulmonary exercise testing (CPET) has been central to preoperative risk assessment before lung cancer surgery since publication of the European Respiratory Society and European Society of Thoracic Surgeons guideline in 2009. The guideline has recently been updated, incorporating ventilatory efficiency expressed as the ventilation to carbon dioxide production slope (VE/VCO_2 slope) and revised thresholds for risk stratification (Figure 1a). We aimed to determine how application of the 2025 CPET algorithm reclassifies physiological risk compared with the 2009 version, and to assess clinical consequences in terms of major postoperative complications across risk categories.

Methods

We retrospectively analysed 506 patients who underwent CPET during evaluation for suspected or confirmed lung cancer between 2008 and 2020. Risk categorisation was applied according to both the 2009 and 2025 European Respiratory Society and European Society of Thoracic Surgeons CPET algorithms. In patients proceeding to lobectomy (n = 138), we compared discrimination and predictive values for major pulmonary complications or death within 30 days.

Results

Risk distribution changed substantially after application of the updated algorithm (Figure 1b). Among those classified as high risk by the 2025 algorithm (n = 127), 91% were newly identified, primarily due to VE/VCO_2 slope greater than 40. In the lobectomy subset, the area under the receiver operating characteristic curve was 0.61 for the 2025 algorithm and 0.57 for the 2009 algorithm (p = 0.998). Sensitivity, specificity and positive/negative predictive values are presented in table 1.

Conclusions

The updated guideline substantially redistributes patients across risk categories and identifies a larger group of physiologically vulnerable individuals, largely driven by ventilatory inefficiency. Overall discrimination between low and intermediate risk remained modest and similar to the 2009 algorithm. The broader high risk category may support perioperative planning, although its calibration and clinical interpretation warrant careful consideration.

Sex Differences in Preoperative Functional Capacity and Postoperative Risk After Lung Cancer Surgery

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Background

Sex differences in postoperative outcomes after lung cancer surgery are well documented, yet the influence of preoperative functional capacity on surgical selection and postoperative risk remains unclear. This study examined sex differences in preoperative cardiopulmonary exercise testing (CPET) performance in patients excluded from surgery due to functional limitations and in those accepted for surgery. We further assessed whether sex independently predicts major pulmonary complications (MPC) or 30-day mortality after adjustment for CPET-derived variables.

Methods

In 498 patients referred for CPET (2008–2020), reasons for non-surgical management were reviewed. CPET variables included weight-indexed VO_2peak, percent-predicted VO_2peak, and VE/VCO_2 slope. Logistic regression evaluated associations between sex and outcome in patients who underwent lobectomy, with sequential adjustment for surgical extent, comorbidities, and CPET results.

Results

Of 498 evaluated patients, 224 underwent resection (52 sub lobar, 149 lobectomies, 23 pneumonectomies). Patients denied surgery for functional limitations (n=91) had markedly lower VO_2peak and percent-predicted VO_2peak than operated patients (table 1). Women excluded from surgery on average reached 80% predicted VO_2peak and VE/VCO_2 slope 35.8, similar to men undergoing lobectomy (78%, VE/VCO2 slope 35.1). Male sex was associated with increased postoperative risk (OR 3.15, 95% CI 1.39–7.16), persisting after adjustment for comorbidities and surgical extent (OR 2.69, 95% CI 1.11–6.50) but abolished after inclusion of percent-predicted VO_2peak (OR 1.39, 95% CI 0.51–3.77).

Conclusions

The excess postoperative risk observed in men after lung cancer lobectomy, appears largely mediated by poorer relative aerobic capacity (% predicted VO_2peak). Reliance on weight-indexed VO_2peak in patient selection may allow physiologically frail men to undergo major surgery while excluding women with comparable or superior functional reserve. This finding is crucial as the latest ERS/ESTS guidelines have removed percent-predicted VO_2peak from their algorithms relying solely on weight-indexed VO_2peak, an approach that may perpetuate sex-related bias in surgical selection.

Magnitude of Triglyceride Reduction and Cardiovascular Outcomes After Myocardial Infarction: A SWEDEHEART Registry Analysis

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Background and aim: Despite causal inference from genetically higher triglyceride levels and cardiovascular risk, therapeutic triglyceride lowering has yet to demonstrate cardiovascular benefits. Providing insights into the magnitude of treatment effect needed and the type of patients who might benefit we assessed the relationship between triglyceride levels and cardiovascular events following myocardial infarction (MI).

Methods: Between 2005–2022, 51,719 MI patients in Swedish MI registry SWEDEHEART were studied. Triglyceride change from admission to 1-year and 1-year levels were evaluated in adjusted Cox models. Outcomes were MACE (all-cause mortality, non-fatal MI, and non-fatal ischemic stroke), all-cause mortality and non-fatal MI.

Results: Over 5.6 years, 9,008 patients experienced a MACE and 5,148 died. Median triglycerides were 1.4 mmol/L (interquartile range IQR 1.0–2.0) at MI admission and 1.2 mmol/L (0.9–1.6) at 1 year. Patients in the top quartile of triglyceride reduction (≥0.6 mmol/L, median 1.0 mmol/L) had highest baseline triglycerides of 2.2 mmol/L (1.8–2.9). Compared to patients with minimal change, this quartile had lowest risk of MACE (HR 0.85 95% CI 0.79-0.92), all-cause mortality (HR 0.90, 0.81-0.99), and non-fatal MI (HR 0.83, 0.74-0.94). Patients in the lowest quartile at 1-year (<0.9 mmol/L) had lowest cardiovascular risk.

Conclusions: Among MI patients, triglyceride reductions of ~1.0 mmol/L were associated with lowest cardiovascular risk. Only 27% of patients achieved this reduction with baseline triglycerides ~2.2 mmol/L. These findings may explain neutral results in prior triglyceride-lowering trials and suggest future trials should enroll patients with baseline triglycerides ≥2.2 mmol/L and target reductions ≥1.0 mmol/L.

Prevalence and severity of self-rated fatigue at 7 and 24 months and changes over time after survival from cardiac arrest

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Background: The updated post-resuscitation care guidelines report that up to 70% of cardiac arrest survivors experience fatigue symptoms. Physical, cognitive, and mental fatigue are the most assessed dimensions of fatigue. There is currently limited knowledge about the prevalence of the different dimensions of fatigue, the severity of fatigue and the consequences of fatigue following cardiac arrest, and whether it changes over time on an individual level. The aim was therefore to investigate the prevalence and severity of self-rated fatigue symptoms at 7 and 24 months after out-of-hospital cardiac arrest (OHCA) and changes over time.

Methods: This is a longitudinal prospective study, including data from a sub-study of the Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2) trial at 8 sites in Sweden, Denmark, and the United Kingdom. The 20-item Multidimensional Fatigue Inventory (MFI-20) was used to assess self-rated fatigue. The questionnaire consists of five dimensions: General fatigue, Physical fatigue, Mental fatigue, Reduced activity, and Reduced motivation. Total scores were calculated for each dimension separately. Scores ≥13 indicate severe–very severe fatigue symptoms.

Results: 82/106 (77%) OHCA survivors completed the MFI-20 at both 7 and 24 months. Most OHCA survivors were men (88%). At 7 and 24 months post-OHCA, 27% versus 32% of the survivors reported severe–very severe General fatigue. Severe–very severe Physical fatigue was most common (43% versus 39%), and Reduced motivation least common (10% versus 12%) (Table 1). Despite individual changes (Figure 1), the fatigue symptoms remained over time on a group level with no significant changes in any of the five dimensions (p=0.144–0.854).

Conclusion: This long-term follow-up indicates a need of individualized follow-up of fatigue symptoms after OHCA at different timepoints. The findings support both early and late screening and tailored post-OHCA interventions to help survivors managing their fatigue.

Understanding sexual health trajectories in patients with heart failure: A longitudinal analysis

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Background: Sexual health is an important aspect of well-being, yet many patients with heart failure (HF) experience sexual difficulties. Understanding the prevalence, recurrence, and predictors is essential for holistic care. Therefore, in this study we aim to describe the trajectory of sexual health difficulties over one year and identify predictors of recurrent difficulties.

Methods: Data from the HF-Wii study were analyzed at baseline, 3, 6, and 12 months. Sexual health was assessed using one-item from the Minnesota Living with Heart Failure questionnaire: “Did your heart failure prevent you from living as you wanted during the past month by making your sexual activities difficult?” (0=no difficulties; 5=very much difficulties). Patients were classified as having no difficulties (score 0) or difficulties (score 1–5). Over time, they were grouped as having no sexual difficulties during the 4 measurements (0–1 occurrence) or recurrent difficulties (2–4 occurrences). Baseline demographics, clinical data, anxiety and depression (HADs) were collected. Logistic regression identified predictors.

Results: Of 373 patients (mean age 66±12; 27% women), 76% were married/in a relationship; 72% NYHA I/II. At baseline, 66% reported sexual difficulties. Among these, 64% experienced difficulties at all follow-ups, and 29% at 2–3 follow-ups. Of those without baseline difficulties, 50% remained free of difficulties, while 15% reported them at all follow-ups. Persistent difficulties were associated with male gender (OR 4.98, p<.001), anxiety (OR 3.29, p=.002), depression (OR 3.51, p=.017), being married/in a relationship (OR 2.24, p=.003), higher NYHA class (OR 2.02, p=.005), and diabetes (OR 2.22, p=.029). Explained variance: 31%.

Conclusions: Sexual difficulties are frequent and recurrent throughout the disease trajectory in patients with HF. Male gender, relationship status, psychological symptoms, higher NYHA class, and diabetes increase risk of recurrent difficulties. Routine assessment and open discussion of sexual health should be integrated into cardiac care.

Left Atrial Strain and Stiffness in Patients with Early Onset Atrial Fibrillation: Evidence of Preserved Function Despite Structural Enlargement

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Background

Atrial fibrillation (AF) increases the risk of stroke, heart failure, cardiovascular disease and mortality. Early onset AF may develop cardiac remodeling, but it remains unclear whether patients without structural heart disease have a truly healthy cardiac phenotype. AF could indicate subtle functional abnormalities despite preserved ventricular function and normal atrial size. This study aimed to assess left atrial (LA) function and size in patients under 50 years with newly diagnosed AF.

Methods

We included 60 patients from the PRAY (Progression of Atrial Fibrillation in Young) cohort under 50 years of age (15 women, 45 men), diagnosed with AF within the preceding year. Echocardiography with speckle-tracking was performed at inclusion. Measurements included LA volume index, reservoir, conduit, and booster strain, as well as LA stiffness index. Left ventricular (LV) systolic function was assessed by ejection fraction (EF) and global longitudinal strain (GLS), while diastolic function was evaluated using Doppler-derived indices. Patients with poor image quality or AF during image acquisition were excluded from strain analysis. Data were compared with published reference values to identify early functional impairment.

Results

LA enlargement was observed in 65% of patients. Despite this structural alteration, LA reservoir strain remained within the normal range in 76% of patients, conduit strain in 95%, and booster strain in 84%. LA stiffness index was normal in 94% of cases. Mean LV GLS was 19 ± 3%, with reduced values observed in 42 % of patients. LV systolic function, expressed as EF, was generally preserved, with a mean LVEF of 57 ± 6 %, nine patients demonstrated reduced EF

Conclusion:

In patients with newly diagnosed AF, LA enlargement is common, but LA function is largely preserved. Subtle LV dysfunction, indicated by reduced GLS despite normal EF, occurs in a significant proportion, suggesting early ventricular involvement rather than marked atrial impairment.

Increasing high-sensitivity cardiac troponin I levels are associated with coronary artery calcification: results from the pre-SCAPIS study

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Background: Low values of high-sensitivity cardiac troponin I (hs-cTnI) have previously shown to be associated with coronary artery calcification (CAC). However, prospective studies on the relationship between hs-cTnI and CAC in the general population are scarce. The aim of this study is to evaluate the association between longitudinal hs-cTnI trends and CAC.

Methods: Data were collected from the Northern Sweden Health and Disease Study (NSHDS) and the Swedish CardioPulmonary bioImage Study (SCAPIS), with a mean follow-up period of 15.7 (SD 7.6) years. Hs-cTnI was measured at baseline and follow-up, together with CAC assessment at follow-up among individuals without known cardiovascular disease. Troponin delta was calculated and categorized as Stably low, Stably high, Increasing, and Decreasing. Increased hs-cTnI was defined as ≥ 3ng/L. CACS was categorized as CACS =0, 1–100, and >100.

Results: Among 1,895 participants, women comprised 51% of the study population, the mean age was 42 years (SD 7.7). N=1,325 individuals had stably low troponin, n=197 stably high, n=274 showed an increase and n=99 had decreasing troponin levels. In a logistic regression model adjusting for cardiovascular risk factors and follow-up time, increasing troponin dynamics were associated with elevated CACS. Compared to the stably low reference group, individuals with increasing troponin levels were associated with higher odds of calcification (OR 1.42, 95% CI 1.05–1.92). In stratified analysis with CACS >100, an association was observed for individuals with increasing troponin levels and CACS >100 (OR 1.91; 95% CI 1.23–2.98) compared to the reference group. No associations were observed for other troponin delta groups.

Conclusion: Increasing hs-cTnI was independently associated with the presence of coronary artery calcification and further linked to increased coronary calcification severity in individuals free of known cardiovascular disease.

Bone Morphogenetic Protein 10 and One-Year Outcomes After Open Revascularization in Symptomatic Peripheral Arterial Disease and Carotid Stenosis

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Background: Bone morphogenetic protein 10 (BMP10) has atrial-specific and vascular properties and may link atherosclerosis with cardiac disease. We evaluated whether preoperative BMP10 levels were associated with new-onset atrial fibrillation (AF), major adverse cardiovascular events (MACE), and mortality after open revascularization for symptomatic peripheral arterial disease (PAD) or carotid stenosis (CS).

Methods: We enrolled patients scheduled for endarterectomy for symptomatic PAD or CS. Preoperative plasma BMP10 concentrations were measured using Luminex. Outcomes (new-onset AF, MACE, and all-cause mortality) were obtained from medical records at 1-year follow-up. Associations between BMP10 and outcomes were assessed using Cox proportional hazards regression.

Results: Of 234 enrolled patients, 210 had biomarker and one-year follow-up data available and were included in the analyses; 63% were men and 61% underwent surgery for PAD (61%). Women were generally older than men (median age 77 [IQR 7] vs. 75 [IQR 10], p=0.046) and had higher preoperative BMP10 levels (p=0.045). There were 40 patients with preoperative AF, and at 1 year follow-up, 10 patients had developed new-onset AF, 26 experienced a MACE, and 13 died.

In unadjusted Cox regression, higher BMP10 levels were associated with MACE (HR 1.01, 95% CI 1.00-1.03; p=0.047) and mortality (HR 1.03, 95% CI 1.01-1.04: p<0.001), but not with new-onset AF (HR 1.00, 95% CI 0.97-1.03; p=0.8). Associations with MACE and mortality remained significant after multivariable adjustment.

Conclusions: Higher preoperative BMP10 levels were associated with increased 1-year risk of MACE and mortality, but not new-onset AF, in patients with indication for endarterectomy for PAD or CS. Preoperative BMP10 may complement conventional risk stratification and should be validated in larger cohorts.